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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,402	01/13/2006	Koji Ukai	0425-1242PUS1	9872

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EXAMINER	
HUANG, GIGI GEORGIANA	
ART UNIT	**PAPER NUMBER**
1612	

NOTIFICATION DATE	DELIVERY MODE
03/19/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/564,402	UKAI ET AL.	
	Examiner	Art Unit	
	GIGI HUANG	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,6 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The response filed December 22, 2008 has been received, entered and carefully considered. The response affects the instant application accordingly:

   a. Claims 1-2, 4, and 8 have been amended.

   b. Claims 3, 7, and 9 have been cancelled.

2. Claims 1-2, 4, 6, 8 are pending in the case.

3. Claims 1-2, 4, 6, 8 are present for examination.

4. The text of those sections of title 35.U.S. Code not included in this action can be found in the prior Office action.

5. All grounds not addressed in the action are withdrawn or moot.

6. New grounds of rejection are set forth in the current office action.

New Grounds of Rejection

7. Due to the amendment of the claims the new grounds of rejection are applied:

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-2, 4, 6, 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite that the "first granule contains seeds" which is unclear as a granule is typically with one seed and the requisite active and/or excipients and the specification (page 10-11) addresses the granule with the active agent with one seed being coated the grouping of seeds together are multiple (granules). It is unclear what is meant by the recitation. It does not allow one of skill in the art to ascertain the metes and bounds of the invention. For purposes of prosecution, the first granule is view with any number of seeds.

10. Claims 1-2, 4, 6, 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite that the thickening agent to be from the group consisting of methyl cellulose, propylene glycol alginate, xanthan gum, purified gelatin, hydroxypropyl cellulose, hydroxypropylmethyl cellulose, polyvinyl alcohol, polyvinylpyrrolidone (PVP), sodium polycarboxymethyl cellulose (CMC-Na), macrogol and povidone. The recitation is confusing as povidone and PVP are the same. It is unclear if the same or another polymer was intended. It does not allow one of skill in the art to ascertain the metes and bounds of the invention. For purposes of prosecution, the povidone and PVP are viewed as the same.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and

the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claim 1-2, 4, 6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Depui et al. (WO 97/25066) in view of Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition).

Depui et al. teaches a pharmaceutical dosage form comprising proton pump inhibitors, bases (antacid agents), alginates, thickeners, polymers (including enteric polymers), and other pharmaceutical excipients to form multilayered tablets, sachets, and multiple unit tableted dosage forms. Depui also teaches that the sachet form can comprise the coated proton pump inhibitor pellets with an alginate optionally mixed with excipients. The proton pump inhibitors may be utilized in neutral or salt forms, including racemic form or pure form. The specific proton pump inhibitors taught are omeprazole (and encompassing its optical isomer esomeprazole), lansoprazole, pantoprazole, and pariprazole (rabeprazole). The proton pump inhibitors are in granular form, individually enterically coated with a polymer (including hydroxypropyl methylcellulose), and combined with alginate/antacid agent powders or granules and other excipients to be compressed into a tablet. The multiple unit dosage form is also taught to be dispersed in liquid and can be given to patients with swallowing disorders. The formulated core material is in a granules size approximately between 0.1 and 4mm and preferably between 0.1 and 2mm.

Depui teaches the prepared active pellets/granules comprising omeprazole, hydroxypropyl methylcellulose and Polysorbate 80, and can be further combined with calcium carbonate (base), magnesium hydroxide (base), potato starch (glidant, diluent,

disintegrant and binder), water, microcrystalline cellulose, crosslinked polyvidone (polyvinylpyrrolidone). Depui also teaches the antacid or alginate granules comprise mannitol, corn starch, potato starch, low-substituted hydroxypropylcellulose (thickening agent), microcrystalline cellulose, and crosslinked PVP. Depui also teaches the inclusion of additives for the granules including plasticizers, pigments, anti-tacking and anti-static agents such as talc and magnesium stearate. Depui teaches the inclusion of layer substances for antacid formulations for improved properties such as pH-buffering with components such as citric acid and talc (Abstract, Page 2, lines 5-10, Page 3, lines 10-18, Page 4, lines 15-21, Page 5, lines 15-30, Page 6, lines 1-29, Page 7, lines 1-20, Page 8, lines 20-25, Page 9, lines 1-10, Page 10 (all), Page 11, lines 10-15, Page 12, lines 12-30, Page 13, lines 1-2, 25-30, Page 14, lines 9-25, Page 16, lines 1-24, Page 19, lines 5-20, Page 21 line 5-28, Page 22, lines 14-15, Example 1, Page 23 (all), Page 25-26, Example 2, Page 27-28, Example 3, Page 29, Example 4, Claim 1-8, 13-15, 17-18, 20-23). It is noted that the recitation of intended use or intended properties of the intended used do not have patentable weight in a composition claim.

Depui et al. does not expressly teach the incorporation of light anhydrous silicic acid (silicone dioxide).

Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition) teaches the benefits of antiadherents and glidants in formulations. Pharmaceutical Dosage Forms teaches that talc, Cab-O-Sil, and Syloid are analogous materials for both antiadherent and glidant properties. It also teaches that silica has greater efficiency as a glidant than magnesium stearate or purified talc.

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute light anhydrous silicic acid for talc or magnesium stearate, as suggested by Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition), and produce the instant invention. It would have been obvious to substitute one analogous material for another depending on the desired flow property and adhesion for the product.

One of ordinary skill in the art would have been motivated to do this because it is desirable for manufacturers to have analogous choices to substitute the antiadherent and/or glidant when motivated by pricing, availability, or desired properties of the antiadherent and glidant used to produce the final product.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claim 1-2, 4, 6, 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ukai et al. (U.S. Pat. Pub. No. 2002/0039597) in view of Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition) and Samejima et al. (U.S. Pat. No. 5068112).

Ukai et al. teaches a composition comprising benzimiadzole type compounds and its alkali salts-all are proton pump inhibitors, bases, thickeners, polymers (including

enteric polymers), and other pharmaceutical excipients that are formed into tablets or granules soluble or rapidly degradable (dispersible) in water or in gastric acid. The specific proton pump inhibitors taught are omeprazole (and encompassing its optical isomer esomeprazole), lansoprazole, pantoprazole, and rabeprazole. The proton pump inhibitors are in granular form, individually enterically coated with a polymer (including hydroxypropyl methylcellulose), and combined with bases, crospovidone. The active and coating can be laminated on seed granules. Additionally, granules not containing the proton inhibitors ("placebo") and be formed blend with other excipients, and be combined with the active granules to be compressed into a tablet. The formulated core material is made, granulated, dried, and screened through a 24-mesh screen, producing particle sizes of about 841 micron or less (see STG Particle Size/Screen Mesh Comparison).

Tables 6-13 (Pages 6 -8) and Examples 28-29 provide several examples, fulfilling the claims. Ukai teaches the prepared active granules comprising sodium rabeprazole, carbonate, mannitol, and hydroxypropyl cellulose. The granule without the proton inhibitor has mannitol and hydroxypropyl cellulose (also a thickener) with variation. Crospovidone, talc, and HA Sankyo (contains talc, fumaric acid, and hydroxypropylmethyl cellulose) are also added with other excipients to form the placebo (Abstract, Paragraph 2, 4, 7, 9-14, 17, 20-21, 25-26, 29-33, 40-43, 72-82, Claims 1-15). It is noted that the recitation of intended use or intended properties of the intended used do not have patentable weight in a composition claim.

Ukai et al. do not expressly teach the incorporation of anhydrous silicic acid (silicon dioxide) or citric acid.

Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition) teaches the benefits of antiadherents and glidants in formulations. Pharmaceutical Dosage Forms teaches that talc, Cab-O-Sil, and Syloid are analogous materials for both antiadherent and glidant properties. It also teaches that silica has greater efficiency as a glidant than magnesium stearate or purified talc.

Samejima et al. teaches that known buffers for pharmaceutical preparations such as granules are organic acids such as fumaric acid, succinic acid, citric acid, and malic acid (Col. 2, lines 5-21 and 34-36).

It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute light anhydrous silicic acid for talc or magnesium stearate, as suggested by Pharmaceutical Dosage Forms: Tablets (Vol.1, Second edition) and substitute citric acid for fumaric acid as suggested by Samejima, and produce the instant invention. It would have been obvious to substitute one analogous material for another depending on the desired flow property, adhesion, or amount of buffering for the product.

One of ordinary skill in the art would have been motivated to do this because it is desirable for manufacturers to have analogous choices to substitute the antiadherent/glidant or buffers when motivated by pricing, availability, or desired properties of the antiadherent, glidant, and buffer used to produce the final product.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to Arguments

14. Applicant's arguments in regards to the intended activity of mannitol are not persuasive as it is not commensurate in scope with the claims, and as the claims are composition claims the recitation of intended use does not have patentable weight.

15. In regards to Applicant's arguments filed 12/22/2008 that the Examiner did not properly resolve the Graham factors citing the rationale for combining the references is improper, has been fully considered but is not persuasive. The Examiner cited the teachings of Depui et al. where the excipients talc and magnesium stearate are used, and Pharmaceutical Dosage Forms teaches that the that talc, Cab-O-Sil, and Syloid are analogous materials in formulations and are known in the art, as well as that silica has greater efficiency as a glidant than magnesium stearate or purified talc which provides motivation and what is the reasonable expectation of success for its use. Thereby the factors have been met (e.g. Page 14 of Applicant's arguments for Graham factors a-d).

This is also the case with Ukai et al. which taught that fumaric acid, talc, and magnesium stearate are used, and Pharmaceutical Dosage Forms teaches that the that

talc, Cab-O-Sil, and Syloid are analogous materials in formulations and are known in the art, as well as that silica has greater efficiency as a glidant than magnesium stearate or purified talc which provides motivation and what is the reasonable expectation of success for its use. Thereby the factors have been met (e.g. Page 14 of Applicant's arguments for Graham factors a-d). This also applies to Samejima et al. who taught that known buffers for pharmaceutical preparations such as granules are organic acids such as fumaric acid, succinic acid, citric acid, and malic acid are analogous and simple substitution for one known element such as citric acid for another such as fumaric acid to obtain predictable results is obvious and well within the skill of one of the art as it taught in the art. The argument is thereby not persuasive.

16. In regards to the argument of Depui being silent on the second granule having an active, Depui teaches embodiments with two granules (proton inhibitor pellets and antacid/alginate pellet) combined together in the sachet with excipients and is thereby not persuasive. The recitation of what the function of a component is in the composition is not persuasive as if the composition contains the component, the composition recitations are met.

17. Applicant's arguments for Ukai are that the active is not on the seed are not persuasive as Ukai teaches that it can be laminated on seeds.

Conclusion

18. Claims 1-2, 4, 6, 8 are rejected.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GIGI HUANG whose telephone number is (571)272-9073. The examiner can normally be reached on Monday-Thursday 8:30AM-6:00PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fredrick Krass can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

GH
/Zohreh A Fay/
Primary Examiner, Art Unit 1612